

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 38506-0025	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US03/38950	International filing date (day/month/year) 10 December 2003 (10.12.2003)	(Earliest) Priority Date (day/month/year) 10 December 2002 (10.12.2002)
Applicant MEDSTAR RESEARCH INSTITUTE		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (See Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____

as suggested by the applicant.



None of the figures

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

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International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-10, and 20-23, with regard to SPP1, MIG, and IP10

Remark on Protest

<input type="checkbox"/>
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The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68
US CL : 435/6

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	US 2003/0148334 A1 (SUN et al) 07 August 2003 (07.08.2003), abstract, Table 1.	1-4, 8-9
X	ZIMMER, R. et al. Expression Profiling and Interferon-beta Regulation of Liver Metastases in Colorectal Cancer Cells. Clinical and Experimental Metastasis. 2002. Vol 19, pages 541-550, see abstract, Fig. 2.	1-4, 8-9
X	LI, S. et al. Regression of Tumors by IFN-a Electroporation Gene Therapy and Analysis of the Responsible Genes by cDNA Array. Gene Therapy. March 2002, Vol 9, pages 390-397, see abstract	1-4, 8-9

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

09 December 2004 (09.12.2004)

Date of mailing of the international search report

06 JAN 2005

Name and mailing address of the ISA/US

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-10 and 20-23, drawn to a method for predicting the likelihood that a subject will develop collaterals by assaying the expression of at least 3 genes.

Group 2, claim(s) 11-16, drawn to a method for predicting the likelihood that a subject will develop collaterals by assaying for a SNP or altered DNA methylation patterns in at least 3 genes.

Group 3, claim(s) 17-19, drawn to a kit comprising oligonucleotides for detecting genes from table 1.

Group 4, claim(s) 24-28, drawn to a method of promoting collateral formation by administering a composition that decreases expression of at least one gene in table 2 and/or increases expression of at least one gene in table 3.

The inventions listed as Groups 1-4 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature is deemed to be the involvement of genes in the development of collaterals. Claim 1, for example, is drawn to a method of assaying the expression level of at least 3 genes in a subject for the purpose of determining likelihood of developing collateral. Such assaying is taught by Zimmer and Thomas, Clinical & Experimental Metastasis, vol. 19, pages 541-550, 2002. Therefore, the claims do not relate to a single general inventive concept as they lack the same or corresponding special technical feature over the prior art.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

For Group 1, it is noted that claims which do not specify any genes from the tables will be searched according to the full scope of the claims. Therefore, the search for claims 1, 2, 8-10, and 20-23 will not be limited to any specific genes, however claim 2 will be limited to searching 3 genes. For claim 5-7, applicant is required to elect a specific combination of genes from the table. The first named species that will be searched with the generic claims will be IP10, MIG, and SPP1. Therefore, if applicant does not elect any additional groups, the generic claims will be searched to their full scope, claims 2-4 will be limited to any 3 genes, and claims 5-7 will be limited to searching IP10, MIG, and SPP1. With regard to claims 2-4, any additional combination of 5, 10, or 20 genes are considered to be a separate species and will require additional fees. Applicant may wish to elect more than one combination of genes, generically for claims 2-4, and specifically for claims 5-7. If so, it is noted that each combination will also be considered a separate species.

For group 2: for claim 13, applicant is required to elect a specific combination of genes from the table. It is noted that claims which do not specify any genes from the tables will be searched according to the full scope of the claims. Therefore, the search for claims 11, and 14-16 will not be limited to any specific genes, however claim 12 will be limited to searching 3 genes. Applicant is requested to indicate the combination of specific genes from table 1 which claim 13 will be limited to. If applicant wishes to further elect any additional combinations from claim 12, applicant may do so, however such is considered a separate species. Further, Applicant may wish to elect more than one specific combination of genes. If so, it is noted that each combination will be considered a separate species.

For Group 3: applicant is required to elect a specific combination of genes from table 1 to which the claimed oligonucleotides will be limited. Applicant may wish to elect more than one combination. If so, it is noted that each combination will be considered a separate species.

For Group 4: applicant is required to elect a specific combination of genes from tables 2 and/ or 3 to which the claims will be limited. Further, for claim 28, applicant is required to indicate a specific gene from table 3 for protein administration. Applicant may wish to elect more than one combination of genes for claims 24 and 28. If so, it is noted that each combination will be considered a separate species.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The genes listed in the various tables are

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drawn to structurally and functionally distinct products. These structurally and functionally different products lack the same or corresponding special technical feature.

Continuation of B. FIELDS SEARCHED Item 3:

Caplus, medline, Genbank

search terms: angiogenesis, collateral, blood vessel, gene, nucleic acid, mRNA, RNA, expression, array, chip, SPP1, IP10, MIG, SCYB10, SCYB9